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EXAMINER	
HAMA, JOANNE	

ART UNIT	PAPER NUMBER
1632	

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Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/736,801	KLEBL ET AL.	
	Examiner	Art Unit	
	Joanne Hama, Ph.D.	1632	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *05 April 2006*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1,3-18,20 and 21* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1,3-18,20 and 21* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Applicant filed a response to the Non-Final Rejection of October 12, 2005 on April 5, 2006. Claims 1, 3-18, 20, 21 are amended. Claims 2, 19, 22 are cancelled.

Claims 1, 3-18, 20, 21 are under consideration.

Withdrawn Objections/Rejections

Claim Objections

Applicant has amended claim 13 to remove "lacuna" and has corrected multiple dependencies in claims 4-17. The claim objections have been withdrawn.

35 U.S.C. § 101

Applicant's arguments, see page 6 of Applicant's response, filed April 5, 2006, with respect to the rejection of claim 19 have been fully considered and are persuasive. Applicant has cancelled claim 19. The rejection of claim 19 has been withdrawn.

35 U.S.C. § 112, 2nd parag.

Applicant's arguments, see page 6 of Applicant's response, filed April 5, 2006, with respect to the rejection of claims 1, 3-18, 21 have been fully considered and are persuasive. Claims 2, 19, 22 are cancelled and the rejections regarding these claims are thus withdrawn. Claims 1, 11, 12, 16, 18

were amended from "compensatingly differentially to "compensating differentially." Applicant amended claim 3 to address that the phrase, "one protein or protein fragment which is endogenous to the organism and/or foreign," is unclear. Applicant amended claim 12 to address that the phrase, "enhanced to control," was unclear. Applicant amended claim 13 to address the phrase, "carried out [lacuna] replacing." Applicant amended claim 14 to address that the phrase, "carried out by enhancing its expression" is unclear. Claim 15 has been amended to address the issue of antecedent basis. Claim 17 has been amended to address the clarity of the phrase, "phenotype organism." The rejection of claims 1, 3-18, 21 has been withdrawn.

35 U.S.C. § 102

Applicant's arguments, see page 6 of Applicant's response, filed April 5, 2006, with respect to the rejection of claims 1, 3-6, 8-10, 15-17 as being anticipated by Fellenberg et al., as evidenced by de Almeida et al. have been fully considered and are persuasive. Applicant indicates that "phenotyping is carried out by measuring the reduction or elimination of compensating differential expression or by labeling at least one compensating differentially regulated gene." Fellenber et al. do not teach that phenotyping involves these steps. The rejection of claims 1, 3-6, 8-10, 15-17 has been withdrawn.

It is noted that the rejection of claim 2, with regard to its rejection as being anticipated by Rohlmann et al. is withdrawn because claim 2 is cancelled.

35 U.S.C. § 103

Applicant's arguments, see page 8 of Applicant's response, filed April 5, 2006, with respect to the rejection of claims 20 and 21 as being unpatentable over Fellenberg et al., in view of Tugendreich have been fully considered and are persuasive. Applicant indicates that Fellenberg et al. does not teach or suggest a transgenic organism having a genetically modified phenotype caused by the reduction or elimination of a compensating differential gene, a limitation written in claims 1 and 18, as a characteristic possessed by the genetically modified organism used in the screens. As such, the rejection as they apply to claims 20 and 21 as being unpatentable over Fellenberg et al. and Tugendreich et al. is withdrawn.

It is noted that the rejection as it applies to claim 19 is withdrawn as the claim has been cancelled.

New/Maintained Rejections

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 1, 3-17, 20, 21 are newly rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of

the claimed invention. This is a new matter rejection. 37 CFR 1.118 (a) states that "No amendment shall introduce new matter into the disclosure of an application after the filing date of the application".

Claim 1, step c, has been amended to include the limitation, "wherein phenotypeing is carried out by the reduction or elimination of compensating differential expression or by the labeling of at least one compensating differentially regulated gene." A search of the specification provides no support for the limitation and Applicant has not indicated where support for this limitation is found. Claims 3-17, 20, 21 depend on claim 1.

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 1, 3-17, 20, 21 are newly rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

According to The American Heritage Dictionary of the English Language, 4th ed. [online], 2000, [retrieved on 2006-06-06]. Retrieved from the Internet <http://dictionary.reference.com/search?r=2&q=phenotype>, "phenotype" means:

1. a. The observable physical or biochemical characteristics of an organism, as determined by both genetic makeup and environmental influences.

b. The expression of a specific trait, such as stature or blood type, based on genetic and environmental influences.

2. An individual or group of organisms exhibiting a particular phenotype.

As this applies to claim 1, step c, the amendment, "wherein phenotyping is carried out by the reduction or elimination of compensating differential expression or by the labeling of at least one compensating differentially regulated gene" is used to describe "phenotyping." However, the claim's definition of "phenotyping" is contrary to the art-accepted use of the term. Further, there does not appear to be support in the specification for the use of "phenotyping" in this manner in claim 1. Claims 3-17, 20, 21 depend on claim 1.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 1, 3-6, 8, 10, 16, 17 remain rejected under 35 U.S.C. 102(b) as being anticipated by Suzuki et al., 2001, Am. J. Physiol., Endocrinol. Metabl., 281: E857-866 for reasons of record, October 12, 2005.

Claims 1, 3-8, 11-14, 17, 18 remain rejected under 35 U.S.C. 102(b) as being anticipated by Rohlmann et al., 1998, J. Clin. Invest., 101: 689-695, as evidenced by Ishibashi et al., 1993, J. Clin. Invest., 1993, 92: 883-893 for reasons of record, October 12, 2005.

Claims 1, 3, 5-9, 15, 17, 19, 20, 21 remain rejected under 35 U.S.C. 102(b) as being anticipated by Tugendreich et al., 1999, Genome Research, 11: 1899-1912 for reasons of record, October 12, 2005.

Response to Arguments

Applicant's arguments filed April 5, 2005 have been fully considered but they are not persuasive.

Applicant provides an argument addressing why Suzuki et al. do not anticipate the claimed invention (Applicant's response, page 7). Applicant indicates that, "phenotyping is carried out by the reduction or elimination of compensating differential expression or by the labeling of at least one compensating differentially regulated gene which is not taught by Suzuki et al." In response, Suzuki et al. teach labeling of at least one compensating differentially regulated gene. Suzuki et al. teach that cRNA used in the microarray study was biotin-labeled (Office Action, page 8, line 7). These cRNA were obtained from fed or fasted MHCα-tTA and HSL-induced HBK-HSL mice. As such, the mRNA obtained from the different mouse populations would comprise differentially regulated genes. Suzuki et al. fits the specification's criteria of a labeled gene: "(a) another possibility is also to label one or more compensatingly upregulated genes by means of a suitable marker/tag (which is coupled to the gene product, for example) (specification, page 6, lines, 4-6)." As such, Suzuki et al., anticipate claims 1, 3-6, 8, 10, 16, 17 and the rejection is maintained.

Applicant provides an argument addressing why Rohlmann et al., as evidenced by Ishibashi et al. do not anticipate claims 1, 3-8, 11-14, 17, 18 (Applicant's response, page 7). Applicant indicates that the double knockout mouse taught by Rohlmann et al. is different from the claimed genetically modified organism wherein the modification must be perceived or measured from the outside of the organism as defined in the application on page 1, lines 33-38, for example. In response, the art does not limit a phenotype to be exclusively a characteristic that is external and visible and nothing in the claims are drawn to this limitation. While one example of a phenotype is something external or visible, the specification, page 5, lines 22-27, does not limit a phenotype as such: "(p)henotyping refers to causing or enhancing a phenotype distinguishable from the wild-type organism in the genetically modified organism." As such, Rohlmann et al. anticipate claims 1, 3-8, 11-14, 17, 18 and the rejection is maintained.

Applicant provides an argument addressing why Tugendreich et al. do not anticipate claims 1, 3, 5-9, 15, 17, 19, 20, 21 (Applicant's response, page 7). Applicant indicates that Tugendreich et al. do not teach a method for generating a genetically modified organism wherein as one of the method steps the phenotyping is carried out by the reduction or elimination of compensating differential expression or by the labeling of at least one compensating differentially regulated gene. In response, Tugendreich et al. teaches yeast comprising an expression construct that overexpressed p38. Tugendreich et al. teach that to overcome the probelm of toxicity caused by expression of p38,

yeast comprising mutations in PTP2 and PTP3 were used (Office action, page 12). As such, Tugendreich et al. anticipate claims 1, 3, 5-9, 15, 17, 19, 20, 21 and the rejection is maintained.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claims 20 and 21 remain rejected under 35 U.S.C. 103(a) as being unpatentable over Rohlmann et al., 1998, J. Clin. Invest., 101: 689-695 in view of Capecchi, 1989, TIG, 5: 70-76 for reasons of record, October 12, 2005.

Response to Arguments

Applicant's arguments filed April 5, 2006 have been fully considered but they are not persuasive.

Applicant provides an argument regarding the rejection of claims 20 and 21 as being unpatentable over Rohlmann et al. in view of Capecchi (Applicant's response, page 8). Applicant indicates that Capecchi does not provide a teaching or suggestion to use a knockout mouse as taught by Rohlmann for screening substances that would have an effect on the function of a heterologous expressed protein or protein fragment. Applicant indicates that it is agreed that

knockout mice are useful in analyzing pathology of diseases and as vehicles for exploring new therapies such as gene therapy, but it well understood in the filed that knockout mice are not a source for primary cell assays for drug screens. In response, the teaching of Capecchi is a generic teaching in the art as to what applications a knockout mouse has, including exploring new therapeutic protocols. Capecchi is not read with the expectation that Capecchi singles out a specific knockout mouse with one specific utility; rather Capecchi is used as guidance for the broad breadth of utility of any knockout mouse. Rohlmann et al. teach one example of a knockout mouse and also indicate that the mouse is useful in elucidating a role of LRP or other essential genes in the formation of atherosclerotic lesions (Rohlmann et al., page 694, 2nd col., 2nd parag, see also Office Action, page 13). With regard to the Applicant's argument that knockout mice are not a source for primary cell assays for drug screens, nothing in claims 20 and 21 indicate that the method was limited to cells. In addition to this issue, the Examiner is not completely clear what is meant by the Applicant's argument that "knockout mice are not a source for primary cell assays for drug screens," as primary cultures can be made from cultures and can be used in testing. For example, Grako et al., 1999, J. of Cell Science, 112: 905-915 teach that dissociated cultures of aortic smooth muscle cells from null mice were compared to parallel cultures from wild-type mice for their ability to proliferate and migrate in response to specific growth factors (Grako et al., abstract). As such, claims 20 and 21 are unpatentable over Rohlmann et al. in view of Capecchi and the rejection is maintained.

Conclusion

No claims allowed.

Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Joanne Hama, Ph.D. whose telephone number is 571-272-2911. The examiner can normally be reached Monday through Thursday and alternate Fridays from 9:00-5:00.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Ram Shukla, Ph.D. can be reached on 571-272-0735.

The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to (571) 272-0547.

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JH

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